THE SERUM TREATMENT OF ERYSIPELAS.

by Frank G. Macnair, M.B.

HISTORICAL NOTE.

The first attempt to produce an antistreptococcic serum for the treatment of erysipelas came from the hands of Charrin and Roger[1] in I895. Cultures of streptococci isolated from cases of erysipelas were grown in bouillon for ten days and this was concentrated by evaporation to one tenth and placed in the autoclave at 115 degrees Cent. Thus they believed that they had preserved the original bacterial substance and its toxins. This was used to immunise a mule, giving 30 ccs. intravenously every second day. After about two weeks the mule was bled and the serum used in doses of about ten to fifteen ccs.. They reported good results, particularly in puerperal septicaemia without peritoneal localisation.

Later Marmorek[2], Aronson[3], Moser[4], Savchenko[5] and numerous other workers in this field reported favourable results with antistreptococcal serum in cases of erysipelas.

More recently Goresco and Popesco[6] reported very hopeful results in severe cases using a polyvalent antistreptococcal serum prepared by the Institute of Sero Vaccines, Bucarest.(Dr J. Cantacuzene) Their report was on some eighty cases with a doseage of one cc. or more daily, the results being very satisfactory in nearly every case. The most marked feature was very often a great improvement in the general condition of the patient even if the temperature re-

by lysis. The local lesion improved rapidly and relapses were rare. Control cases treated with normal horse serum gave negative results.

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THE SERUM TREATMENT OF ERYSIPELAS.

Birkhaug's Antitoxin.

In May 1926 Birkhaug[7] announced the production of an antitoxic serum prepared against the erysipelas streptococcus by a method similar to that employed by Dochez[8] in the making of his scarlet fever antitoxin.

Recent work[9,10,11,12] on the haemolytic streptococcus by serological methods has tended to demonstrate type specificity within this large group. Birkhaug[14] had previously demonstrated by agglutination and absorption that 91.2% of erysipelatous strains of haemolytic streptococci isolated from typical erysipelatous lesions fell antigenically into one group and could be easily differentiated from the strains of other haemolytic streptococci not obtained from cases of erysipelas.

Continuing this work he[13] prepared a toxin from this group of streptococci and using a technique similar to that of the Dick and Schick tests investigated the neutralization of this toxin. He found that it was regularly neutralized by convalescent erysipelas serum and by erysipelas antistreptococcal donkey or rabbit serum and not by Dochez scarlet antistreptococcal serum or normal rabbit or donkey serum. He considered that he had demonstrated the presence of this toxin in the blood serum and urine of cases of erysipelas.

It was found by Rivers and Tillet[15] that injec-

into the skin of normal susceptible rabbits gave rise to lesions which were in some cases similar to human erysipelas. These lesions could be prevented by the previous intra-venous injection, twenty four hours before, of serum from immunized rabbits or donkeys. Local immunity could be produced by infiltrating the skin with immune serum before injecting the streptococci and Birkhaug stated that this immunity was specific for the type of streptococcus used to immunise the animal in the production of the serum. More recent work by Singer and Kaptan, however, would suggest that there is considerable overlapping in the antigenic properties of the various groups of haemolytic streptococci and quite possibly all produce almost the same, if not quite the same, toxin.

Birkhaug[7] reported sixty cases treated by means of his serum with an average single dose of I5ccs. of the concentrated form given as early as possible in the disease and usually not repeated. His results were striking, and in cases treated early consisted in a prompt improvement in toxic depression, a rapid and critical fall in temperature and pulse and a rapid disappearance and fading of the erysipelatous lesion.

Unfortunately, as McCann[16] has since pointed out, he used no controls and therefore his figures are possibly misleading. He does not even state the number of deaths, if any; only that "two were moribund when first visited."

Much the same criticism, inadequate control and failure to realize the variation in the severity of erysipelas from year to year, renders invalid the favourable reports made on a large series of cases by Symmers and Lewis[17] in 1927 and 1928. Though even these workers admit that the serum "only controls the immediate attack, in the majority of cases, and confers no lasting immunity and therefore does not prevent either relapses or recurrences, nor does it lessen complications."

Musser[18], in 1927 described thirty cases with only two deaths, but as he gave no details and did not state the usual mortality for erysipelas in New Orleans, his figures were of little value.

In July 1928 McCann[16] criticized the reports of previous users of the serum and stressed the essentialness of adequate control. He gave his conclusions from the treatment of sixty nine cases very guardedly and insisted that the value or otherwise of the serum was still undetermined. Nevertheless his figures did not seem very favourable to his serum treated cases.

The only further report since 1928 has come from H.B.Cushing[19] of Montreal whose cases were largely children. The sole figure quoted is a mortality of 8% of serum treated cases, but as the numerical proportion of adults to children is not given, this figure is of small worth. He considers that the serum is of little value and "In no case of erysip-

elas of the trunk in an infant was any definite effect of the serum noted, yet these cause almost the whole of the mortality from the disease."

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EXPERIENCE OF THE USE OF THIS SERUM IN THE CITY HOSPITAL, EDINBURGH.

Except in the very young and the very old, erysipelas attacking a previously healthy person is a disease which usually tends towards recovery without any treatment. This recovery, which most often occurs between the third and eighth day, is frequently somewhat dramatic with critical fall in temperature and corresponding improvement in the general condition of the patient. On the other hand the recovery may be much more gradual or may be delayed for weeks. At any stage in the disease the whole progress of the condition may be aborted and the patient recover rapidly for no obvious cause.

It follows that in passing a verdict, favourable or otherwise, on any remedy used to treat the condition we must be extremely careful that we do not lay the responsibility for the improvement on the remedy rather than on the natural course of the disease. The very multiplicity of the local applications, drugs, and sera whose use has been enthusiastically advocated by their various sponsors and then allowed to fall back into oblivion, not standing up to the test of time, should warn us against this danger.

Adequate control of our serum cases is essential and extremely hard to attain. Erysipelas varies in its mortality, severity, and duration with such factors as age, sex, and time of year

Beyond this there is a well marked variation from year to year which must be taken into account.

Using Erysipelas Streptococcus Antitoxin obtained from Parke Davis & Co. a total of 91 cases have been treated in the City Hospital, Edinburgh, up to the end of 1929. The treatment was started in November 1927 and was at first given to all moderate and severe cases, the severity being judged by the temperature and the general condition of the patient rather than by the local lesion. This was continued till about July of the same year when in view of the apparently unsatisfactory results obtained it was given only to very severe cases which were not showing improvement with the ordinary methods or cases of moderate or great severity admitted very early in the disease.

It follows that there is a large number of statistics for the last two months of 1927 and the first six months of 1928 and that since that date cases have been very much more spread out.

To get controls for these cases all the erysipelas charts from January 1925 up to date have been reviewed. Out of this large total a preliminary selection was made including only moderate and severe cases. These were found to amount to over 250.

Each serum case was then taken individually and from these controls one was selected which most resembled it in distribution of the lesion, severity of the disease on admission, age and sex of the

patient and month of admission. Most stress was laid on the distribution of the lesion and it was found possible to allocate in all adult cases a control which was of similar distribution. In the case of those under ten years of age this was not found to be so easy and in two facial cases showing, on admission, spread to the trunk, it was necessary to allocate a control which involved the trunk only. This makes the figures for those under ten years slightly less accurate.

The month of the year was allowed for and with a very few exceptions, again in those under ten years of age, it was found possible to give a control admitted on the same month or one immediately before or after it. Age, especially in the very young, and sex, were likewise taken into account.

As regards variation in severity from year to year or secular variation, it will be realized that while more than half our serum cases are for the first six months of 1928 and the other half for dates previous and subsequent to that, our controls extend from 1925 to 1930. Thus variation from year to year is not quite excluded, but this will be discussed later.

Day of admission would not, at first sight, appear to be of any great importance, but when we remember the home conditions of the patients, varying from case to case, but usually inferior to those of hospital with suitable facilities for good diet and

nursing, it follows that this has to be thought of, though perhaps to a more limited extent.

Apart from the administration of serum all cases were treated alike by the usual symptomatic means. Local applications were limited to soaks of concentrated solution of magnesium sulphate.

In most cases included in this series serum was exhibited intra-muscularly on the day of admission or the day following. The dose in the adult was practically always 20ccs.. In a few cases this, or a smaller dose, was repeated on the following day and the average total doseage per adult patient worked out at 23.2 ccs.. In cases under ten years the dose varied more and was usually 5 to 10 ccs. repeated as the clinical condition seemed to warrant. The average total dose was 13.8 ccs..

STATISTICAL DETAILS OF UNCORRECTED CASES.

Total Number 9I.

Adults.

	Serum Cases.		Control Cases.	
	Cases.	Deaths.	Cases.	Deaths.
Body only,	4	I	4	0
Head only, (face ears and scalp)	66	4	69	0
Head spreading to neck and trunk.	8	0	5	0
Totals	78	5	78	3
Ages of adult deaths.	53-80 yrs.		55-62 yrs.	
Average age of adult deaths.	63 yrs.		59 yrs.	
Case Mortality per cent.	6.4		3.8	

Children. (Under I0 yrs.)

	Serum Cases.		Control Cases.	
	Cases.	Deaths.	Cases.	Deaths.
Body only,	5	I	7	2
Head only, (face ears and scalp)	6	I	6	0
Head spreading to neck and trunk.	2	2	0	0
Totals.	I3	4	I3	2
Ages of child deaths.	6/52, 7/52, 6/I2, 6/I2.		I0 dys.-3/52.	
Average age of child deaths.	4/I2.		2/52.	
Case Mortality per cent.	30.7.		I5.4.	

It is obviously unfair to include in our final figures cases where the serum was solely administered because the patient had passed the usual time of recovery without signs of improvement, or, in view of Birkhaug's statement that the serum must be administered early in the disease, cases where the treatment was not started till after the fourth day.

Omitting these cases we are left with a total of 68.

For table of corrected figures, see next page.

STATISTICAL DETAILS OF CORRECTED CASES.

Total Number 68.

Adults.

	Serum Cases.		Control Cases.	
	Cases.	Deaths.	Cases.	Deaths.
Body only,	3	0	3	0
Head only, (face ears and scalp)	50	I	52	2
Head spreading to neck and trunk,	5	0	3	0
Totals.	58	I	58	2
Ages of adult deaths.	69 yrs.		58-62 yrs.	
Average age of adult deaths.	69 yrs.		58.5 yrs.	
Case mortality per cent.	I.7		3.4	

Children.(Under IO yrs.)

	Cases.	Deaths.	Cases.	Deaths.
Body only,	3	I	6	I
Head only, (face ears and scalp)	5	I	4	0
Head spreading to neck and trunk.	2	2	0	0
Totals.	IO	4	IO	I
Ages of child deaths.	6/52, 7/52, 6/I2, 6/I2.		3/52.	
Average age of child deaths.	4/I2.		3/52.	
Case mortality per cent.	40		IO.	
Total case mortality for all corrected cases.	7.3%		4.4%	

The 91 patients in the uncorrected series received serum on an average of 3.8 days after the onset of the disease. The 68 patients in the corrected series on an average 3.1 days after the onset. In the corrected series the 5 who died received serum on an average of 3.5 days after onset.

The average age of all the adult serum treated patients in the corrected series was 35.9 years and of the controls, 36.1 years. The corresponding figures for the children were 54.9 and 56.8 weeks respectively.

The effect of the serum on the course of the disease in those who survived was considered to be best judged by the temperature chart, the day on which the temperature returned to normal being taken as the end of the condition. Some slight difficulty was experienced in cases where the patient had contracted the erysipelas following an operation for some other condition such as mastoiditis, but this difficulty was overcome by taking into account the local lesion. In nearly all cases the fever from serum sickness could be easily distinguished and was not included in this figure.

Average Duration of Fever in all Patients who Survived.

	Serum Cases.	Control Cases.
Uncorrected	8.8 days.	8.4 days
Corrected.	8.0 "	7.8 "

Of those who died the average survival time from the onset of the disease was as follows.

	Serum Cases.	Control Cases.
Uncorrected.	I5 days.	I6 days.
Corrected.	7 days.	I2 days.

(Note. The difference in survival time between the corrected and uncorrected control cases is of course explained by the fact that serum cases admitted late in the disease have been excluded and their controls which were chosen, so far as possible, from cases also admitted late, have been likewise excluded.)

Clinical Experience.

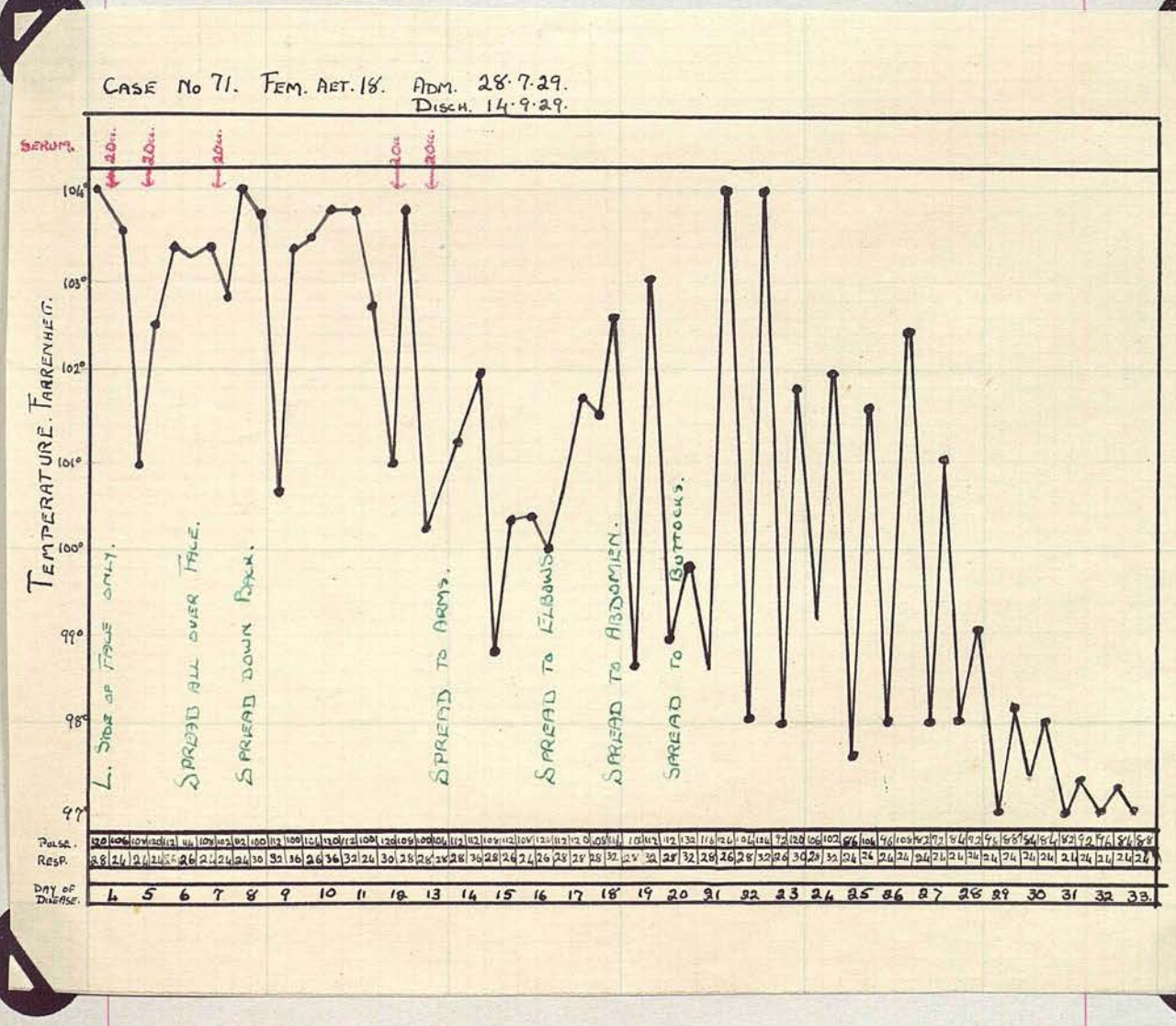
In cases treated early Birkhaug reported a prompt improvement in toxic depression followed by a rapid and almost critical fall in temperature pulse and respiration in twelve to eighteen hours. The most striking clinical effect being a rapid disappearance and fading of the erysipelatous lesion.

This favourable result was quite the exception in our series. For example the case history of a girl of eighteen years of age admitted on the fourth day of disease suffering from acute facial erysipelas will serve to show continued spread in the face of enormous doses of serum.

On admission the lesion involved the left side of the face and neck and the left ear. Her general condition was fairly good but she was obviously very ill with a temperature running between I02 and I04 degrees Fahr. and very marked delirium especially at night.

She was given 20 ccs. of serum intra-muscularly

on admission and this was repeated on the fifth, seventh, twelfth, and thirteenth days. In spite of these enormous doses the erysipelas spread all over the face and down the back of the trunk till it had involved in its passage both arms and the upper part of both thighs. At the same time her fever and delirium continued unabated and her toxic depression was unrelieved.



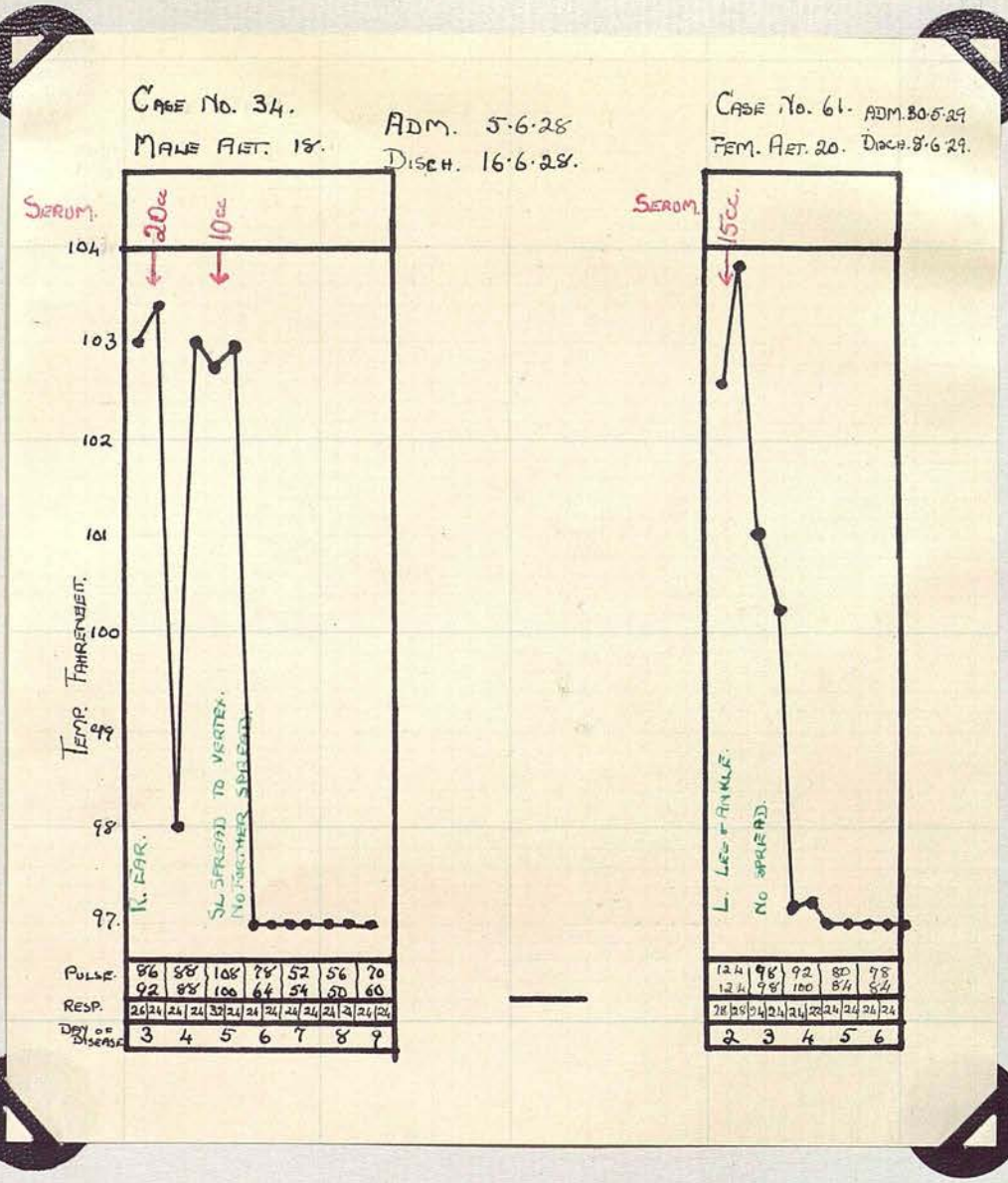
It is perhaps only fair to balance this adverse case report with that of two others which did show a dramatic critical and permanent improvement following

the use of serum, but it must be stressed that these two are the only ones in the whole series which did show such change; the question post hoc ergo hoc remaining unanswered.

Case No. 34. Male aged eighteen admitted on the third day of disease with erysipelas involving the left ear and the skin surrounding it for about one inch. Temperature 103 dgrees Fahr. on admission and patient obviously distinctly ill. 20 ccs. of serum was followed next morning by a temp. drop to 98 degrees and a well marked improvement in the general condition. That night it rose again to 103 degrees with a slight spread of the local process to the vertex. Exhibition of a further 10ccs. was followed by a permanent drop to normal and a cessation of spread.

Case No 61. Female aged twenty admitted on the second day of disease with well marked erysipelas involving the left leg and ankle. Temperature 103.6 degrees on admission and patient obviously ill. 15ccs. of serum was followed by a drop of temp. the next morning to 101 degrees with a marked improvement in the general condition. By the next morning it had dropped to subnormal, where it continued. The local lesion ceased to spread after the administration of the serum.

For charts, see next page.



When we take into account the large bulk of cases in which no such dramatic result was achieved we can only come to the conclusion that results such as these are either the outcome of pure chance, that is, the disease would have aborted at the same time even if serum had not been given, or that they are the result of the non specific element in the serum, in other words, a form of protein shock - a method of treatment much advocated by certain French writers. Possibly, of course, a serum which was not specific for the streptococci in our other cases was specific in these two isolated examples.

In the vast bulk of our cases in addition to not reducing the period of fever, it was found that the spread of the local lesion was unaffected, and that the delirium and toxic depression were unrelieved.

Complications were as frequent in serum treated cases as in controls, the figure for the corrected series being as follows,

	Serum Cases.	Control Cases.
Abcesses.	4	5
Arthritis.	0	I
Nephritis.	2	0
Pericarditis.	0	I

Relapses were more often observed following serum, there being four cases which showed well marked relapse in our serum treated cases with only one case in our controls. One of these four serum treated cases relapsed four times and was over four months in hospital. She was admitted on the fourth day of disease (facial erysipelas) and was given 2occs. of serum on the day of admission and again two days later.

The only benefit which the serum may have conferred was some relief of pain. This statement is based on the experience of the sister in charge of the erysipelas ward. She considered that a few of the serum patients were more comfortable, complained less, and were more tractable. Such benefit, if any, was slight and did not seem to lessen the quantities of hypnotics required in the routine treatment.

COMMENT.

The number of cases in this corrected series, a total of 68, is not large, but so far as possible they have been adequately controlled. We have taken into account and excluded variations due to sex, age, site of disease, month of the year, and day of admission. We have not, on the other hand, taken into account variations in the severity of erysipelas from year to year and this question is deserving of further study.

Our corrected cases were spaced as follows,

	Serum Cases.		Control Cases.	
Year.	No.of cases per year.	Per cent. of total.	No.of cases per year.	Per cent. of total.
I925	0	0	5	7.37
I926	0	0	I6	23.53
I927	6	8.82	22	32.35
I928	45	66.18	4	5.88
I929	17	25.00	21	30.88
Totals.	68	I00.00	68	I00.00

If I928 had been a year during which erysipelas had been more than usually severe our serum figures would have been adversely affected.

On going into the question we find that over the whole of Scotland the deaths per I00 cases notified have not varied very greatly in the last 5 years. The following figures were supplied by the Dept. of Health. Unfortunately the figures for I929 are not yet available.

Table to show Case Mortality for Scotland in the last six years.

Year.	Notifications for Scotland.	Deaths.	Fatality per cent.
I924	29I6	I36	4.663
I925	337I	I50	4.450
I926	3380	I45	4.290
I927	2997	I24	4.I37
I928	3268	I60	4.896

These show that the number of deaths per I00 cases notified was definitely slightly higher in I928 than it had been for some years.

We treated 66.I8% of our total number of serum cases in I928. At that time the deaths per I00 cases over the whole of Scotland were 4.896. Taking 66.I8% of this mortality rate and similarly down the table we get by summation two figures which can be said to compare the death rate per I00 notified cases over the whole of Scotland if such cases had occurred in the same years and proportions as our serum and control cases were taken.

For table, see next page.

Table to show Case Mortality over the whole of Scotland if such cases had occurred in the same proportions and years as our Serum and Control Cases.

Year.	Case Mortality for whole of Scotland.	Serum Cases. Per cent. occurrence of cases each year.	Serum % age x Fatality.	Control Cases. Per cent. occurrence of cases.	Control % age x Fatality.
I925	4.450	0	0	7.37	0.328
I926	4.290	0	0	23.53	I.009
I927	4.I37	8.82	0.364	32.35	I.337
I928	4.896	66.I8	3.240	5.88	0.288
I929 (say)	4.896	25.00	I.224	30.88	I.5I2
			4.828		4.474

This gives a slightly higher case mortality for the whole of Scotland taken in the same proportions as our serum cases over the case mortality taken in the proportion of our control cases, but the difference is so small as to be negligible.

The small difference between these two figures can be contrasted with the actual figures obtained in our series, a fatality rate in serum treated cases of 7.3% and in control cases of 4.4%. The striking similarity between the mortality in our control cases and the mortality over the whole of Scotland should be noted.

The number of cases reported by us is not large and it is therefore dangerous to jump to hasy conclusions as to the death rate per hundered cases from such a series. Nevertheless, insofar as the cause of death from erysipelas is presumably a toxaemic one, the fact that five patients died after the early administration of this so called specific serum is somewhat strong evidence against its antitoxic powers.

That relapses were more frequent in our serum treated cases would suggest that passive immunity conferred by the serum, if any, is of short duration.

The case mortality figures for Scotland can also be taken as a very rough approximation of the severity of the disease. In 1928 it would seem that erysipelas was more fatal than it had been for some

years. It probably follows, therefore, that during that time it was more severe and we would expect that cases which survived would have a longer period of fever. Thus the slight difference between the duration of fever in our serum and control cases (unfavourable to serum treatment) can be considered as of no importance and we can say that as regards duration of fever there is very little difference between our serum treated and control cases.

THE INTRADERMAL USE OF BIRKHAUG'S SERUM IN ADVANCE OF THE SPREADING MARGIN.

Rivers and Tillet,[15] in February 1925, first suggested the local intradermal injection of immune serum in cases of erysipelas.

By injecting rabbits intradermally with haemolytic streptococci isolated from cases of human erysipelas they were able to produce lesions, which in some cases resembled human erysipelas, in spite of the fact that intravenous and intraperitoneal injections of large doses of the same organisms failed to kill. By repeated intracutaneous inoculations they were able to prepare an immune serum from rabbits.

Areas of the abdominal skin of a rabbit were infiltrated with this serum, with normal rabbit serum and with meat infusion and twenty four hours later into each such area, and an untouched area as control, similar doses of streptococci from cases of human erysipelas were injected intradermally.

Skin infiltrated with normal serum or meat infusion was found to be more refractory to infection with haemolytic streptococci than was normal skin. A greater amount of protection against these streptococci was afforded by infiltration with a homologous immune serum and the difference in amount of protection afforded by immune serum over that induced by normal serum could be considered, in their opinion, as representative of the degree of local

passive immunity conferred.

In April 1927 Musser[15] reported fourteen cases where he had used this intradermal injection of Birk-Haug's serum in front of the spreading margin and stated that it was usually effective in stopping the local spread. He did not give any abstracts of his cases.

More recently Montel[20] described a method which he had used for ten years. Three times a day, after washing the skin in front of the advancing margin with boiled water, he carefully dabbed serum on all the limits of the lesion and allowed it to dry. He states that the first application is followed by an intense vascular reaction accompanied by reddening and tension often lasting half an hour and that the results are astounding. In more severe cases he started to use intradermal injection of the serum in front of the spreading margin, thus raising a "véritable barrière antitoxique". Throughout he used the antistreptococcal serum of the Institute of Pasteur but gives no report of individual cases treated.

Other than these two workers no one seems to have taken advantage of Rivers and Tillet's suggestion and it was thought to be worth investigating in suitable cases.

More difficulty was experienced than was expected. In the first place intradermal injection on the face in erysipelas was found to be very painful to the patient and to take a long time to perform,

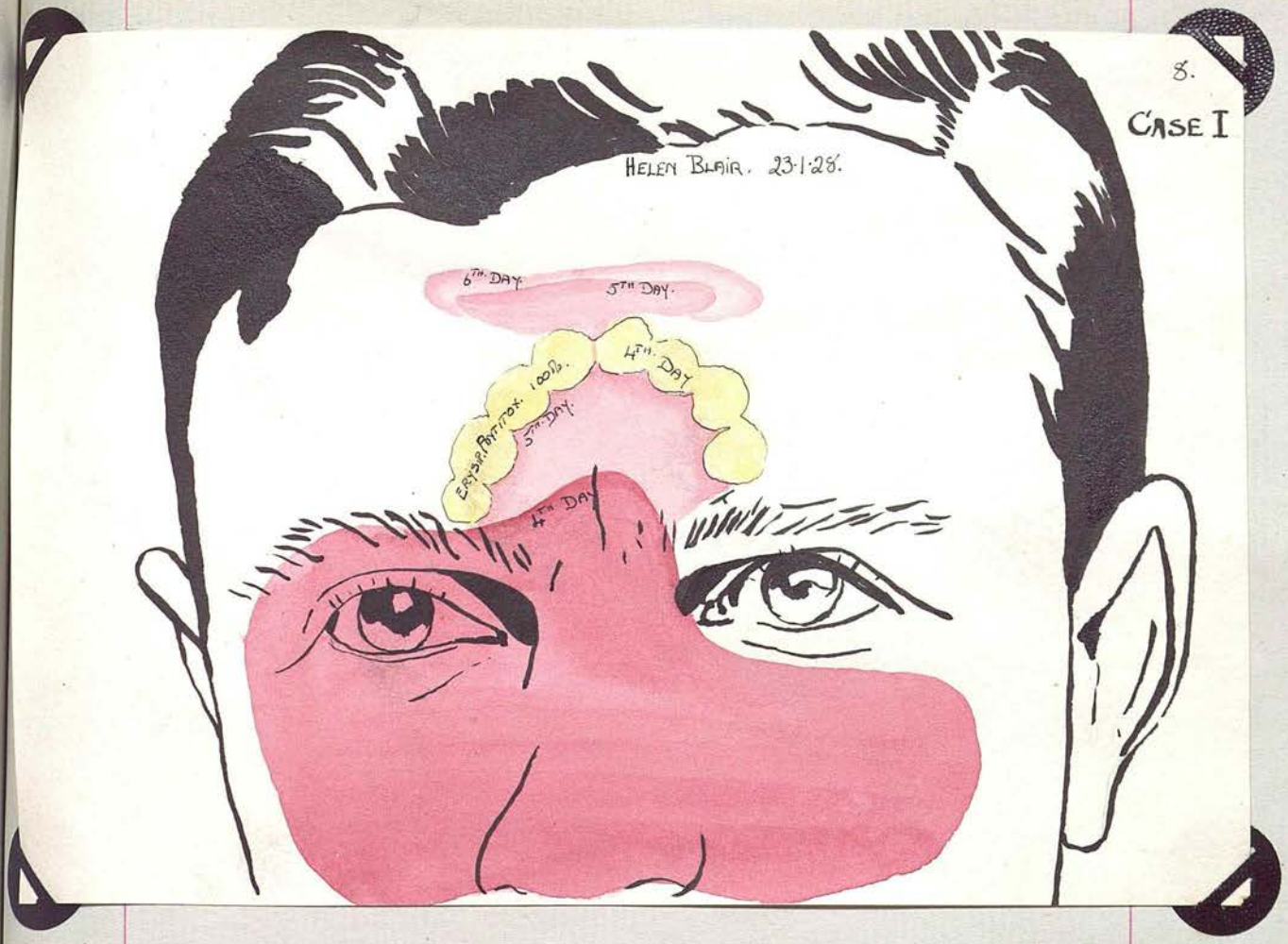
more especially when using the thick concentrated globulin serum. Moreover it was found to be impossible to raise an unbroken weal of serum in lax tissues such as occur round the eye. Nor was injection of the scalp found to be feasible. It follows that the number of cases occuring where an obviously rapidly spreading margin in an area suitable for infiltration is small.

As far as possible in each case the most active limit of the lesion was determined by the local tenderness and other evidence of inflammation and about half an inch in front of this a series of intradermal injections made, each consisting of .I to .3ccs.of concentrated serum or serum diluted one to one with sterile normal saline.

In the first place it was thought to be desireable to see whether the antitoxic serum had any effect when injected thus into an area already actively inflamed. In two cases this was carried out but in both cases no effect could be observed when examined twelve and twentyfour hours later.

Case I: Female aged eighteen. Admitted on the fourth day of disease with facial erysipelas. General condition good. The most actively spreading margin seemed to be just above the root of the nose and half an inch in front of this serum was injected as shown in the diagram. Twentyfour hours later it was found that the erysipelas had spread exactly up

CASE I



to the infiltrated area and was showing it up as a series of flat pale round areas against which on the nasal side the erysipelas stood up red and raised with a crenated border. At one point, where the weal was slightly interrupted, the erysipelas had spread in a thin red line between two adjacent injections and was extending on the forehead. Forty eight hours after the injection there was a further slight spread on the forehead but no where else. The infiltrated area was still unaffected. Thereafter the condition subsided rapidly.

Case 2 : Male aged twenty two, admitted on the fifth day of disease with erysipelas involving the left ear and the left side of the face. General

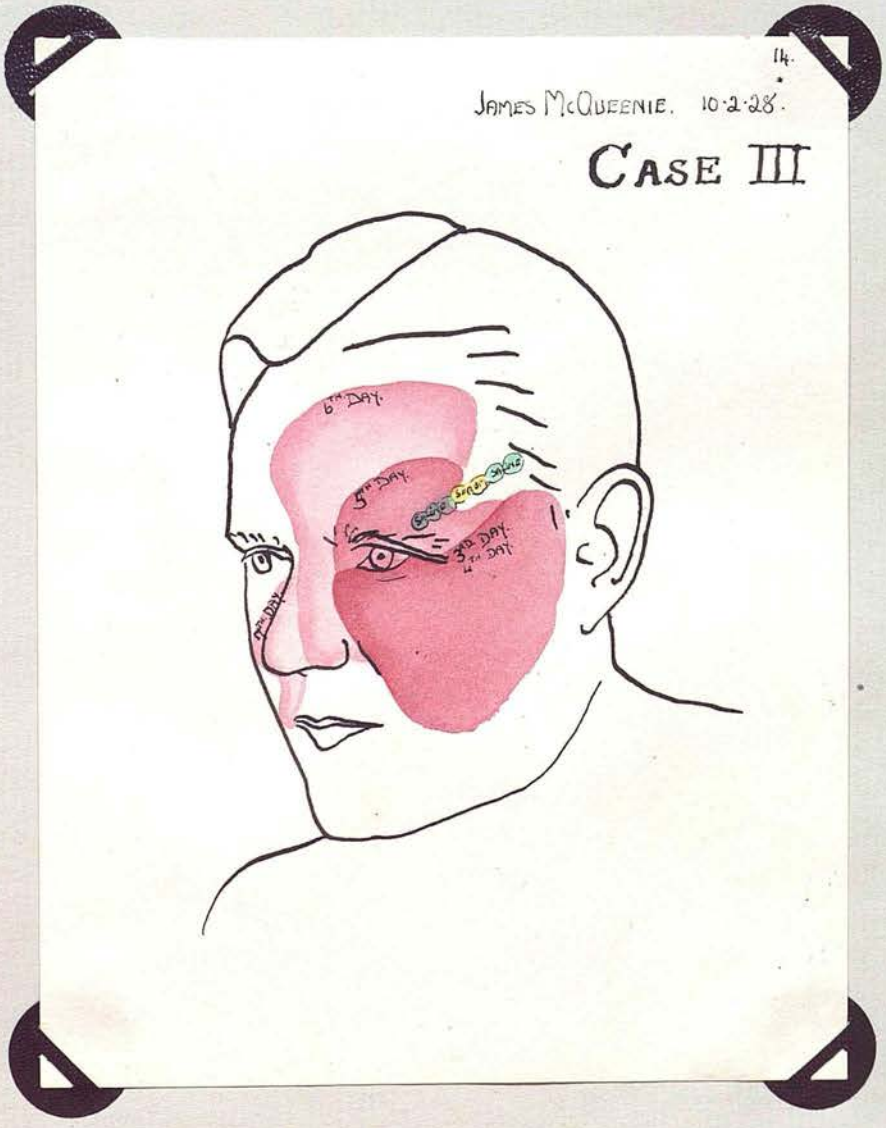
ALEX. MCROSTIE. 8.2.28

CASE II.

condition good. The most active spreading margin seemed to involve the left temple and the left naso-labial fold and half an inch in front of the margin at the left temple a weal of concentrated erysipelas antitoxin was raised as shown in the diagram. Twenty four hours later the erysipelas had spread to the upper lip and up over the right eye to the fore-head. The injected area was nowhere involved but did not stand out as in the last case. Forty eight hours after injection the erysipelas had spread further on the forehead but did not involve the intra-dermal area. Eight days after injection, the

condition having involved the scalp and commenced to subside everywhere, the injected area was still demonstrable as a pale band running across the flushed forehead.

Case 3 : Male aged twenty four admitted on the third day of disease suffering from facial erysipelas of distribution very similar to the last case and with the most actively spreading margin again just below the left temple. General condition good.



Again a weal was raised, a total of six injections being made, but while the central two were of concentrated serum, the outside two on each side

were of normal saline. Twenty four hours later there had been no spread. Forty eight hours later the left eye was involved and the margin passed over the two lowest injections (saline) but did not involve the serum injections. Seventy two hours after injection there had been a slight spread over the forehead but the condition in the infiltrated area was unchanged.

Possibly, therefore, the mechanical action of infiltration was not sufficient to protect the skin against invasion.

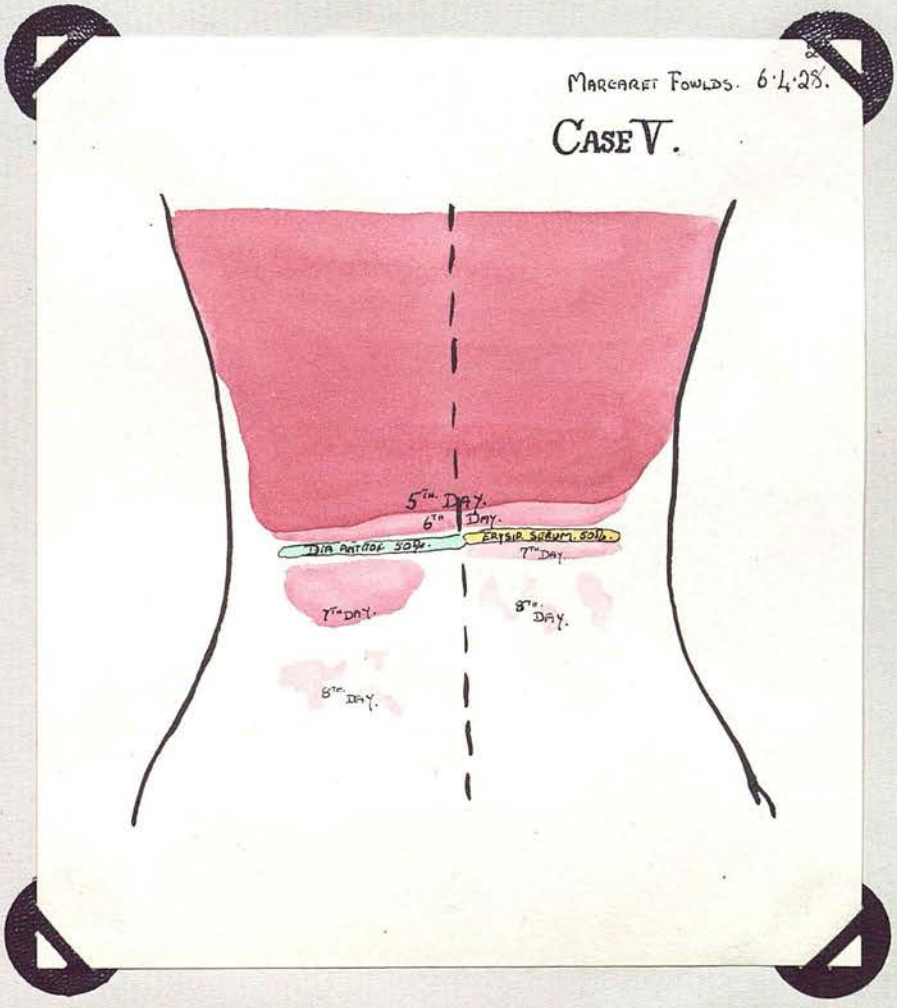
Case 4 : Female aged seventeen admitted on the second day of disease suffering from subacute facial erysipelas. (For diagram see next page.) The most marked spreading edge was judged to be on the left cheek in front of which a serum weal was raised as shown. Twenty four hours later there had been a slight spread towards the infiltrated area, the edge of which could be plainly discerened, and a spread up to the left eye and the root of the nose. Forty eight hours after injection there had been a further slight spread on the forehead but no involvement of the intradermal area. Thereafter the condition subsided rapidly.

Eliz. Flynn. 14.3.28

CASE IV.

Case 5 : Female aged twenty admitted on the third day with facial erysipelas following a mastoid operation. General condition good. In spite of 20ccs. of erysipelas antitoxin given intramuscularly the erysipelas spread rapidly over the face to the other ear and down the back of the neck to the scapular region. On the fifth day of the disease it had spread down the back to the waist and three

quarters of an inch in front of the advancing margin a weal was raised right across the back, using on the left side concentrated diphtheria antitoxin diluted one to one with normal saline and on the right side concentrated erysipelas antitoxin similarly diluted. About three and a half ccs. of the diluted mixture was used on each side and a solid unbroken weal raised.

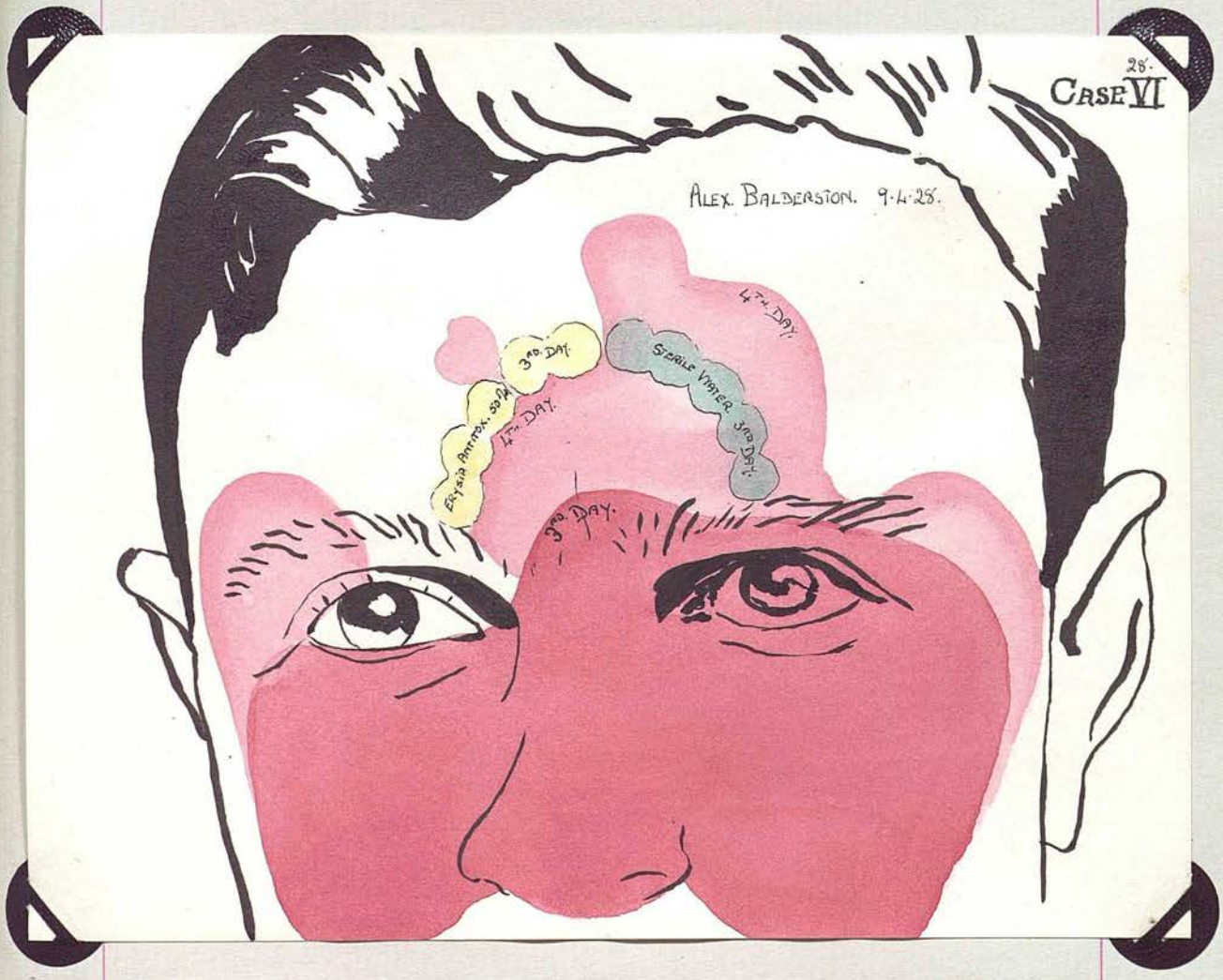


Twenty four hours later the inflammatory process was demonstrable about half an inch in front of the weal on each side though more extensive on the left and on neither side did it look nearly so angry as previously.

Forty eight hours after injection spread was

slight and after that the condition rapidly subsided.

In this case, <u>if</u> the intradermal injections played any part in the abortion of the process, diphtheria antitoxin would seem to ~~be~~ have been almost as effective as the erysipelas antitoxin.



<u>Case 6</u> : Male aged twenty nine admitted on the third day of disease, suffering from facial erysipelas of distribution as shown. General condition fairly good. The most active spreading margin seemed to be at the root of the nose and a series of injections were made in advance of that margin, using on the right side erysipelas antitoxin and sterile water, one to one, and on the left side sterile water

alone. On the left side it was found possible to raise an unbroken weal but on the right this was less successful and the line was broken at more than one point. Twenty four hours later the erysipelas had spread, on the left side to involve the whole of the infiltrated area and the skin of the forehead for about half an inch in front, whereas on the right side it had not extended beyond the injected area except at one point where it had broken through between two injections. The margin between the erysipelas and the infiltrated area was much less defined than in Case I where concentrated serum was used. During the next three days the erysipelas extended all over the scalp but at no time involved the area infiltrated with serum.

Case 7 : Female aged twenty two admitted on the second day of an attack of subacute facial erysipelas following a mastoid operation on the left ear. General condition good. At first only the left ear was involved but the condition gradually spread till on the fourth day of the disease it had reached the side of the face as shown in the diagram. The advancing margin was at no time well defined, nevertheless it was decided to make an attempt to stop the further spread and fifty per cent. serum in sterile normal saline was injected about half an inch in front of the margin as shown. Considerable difficulty was experienced in raising an unbroken weal in the lax tissues at the corner of the eye and it was

realized that there was more than one gap in the barrier at that point. Twenty four hours later the erysipelas had spread up to, but not beyond, the infiltrated area on the left cheek but at the corner of the eye it had spread right over the barrier and involved the skin of both eyelids. For two days it continued to spread over the forehead and then subsided rapidly.

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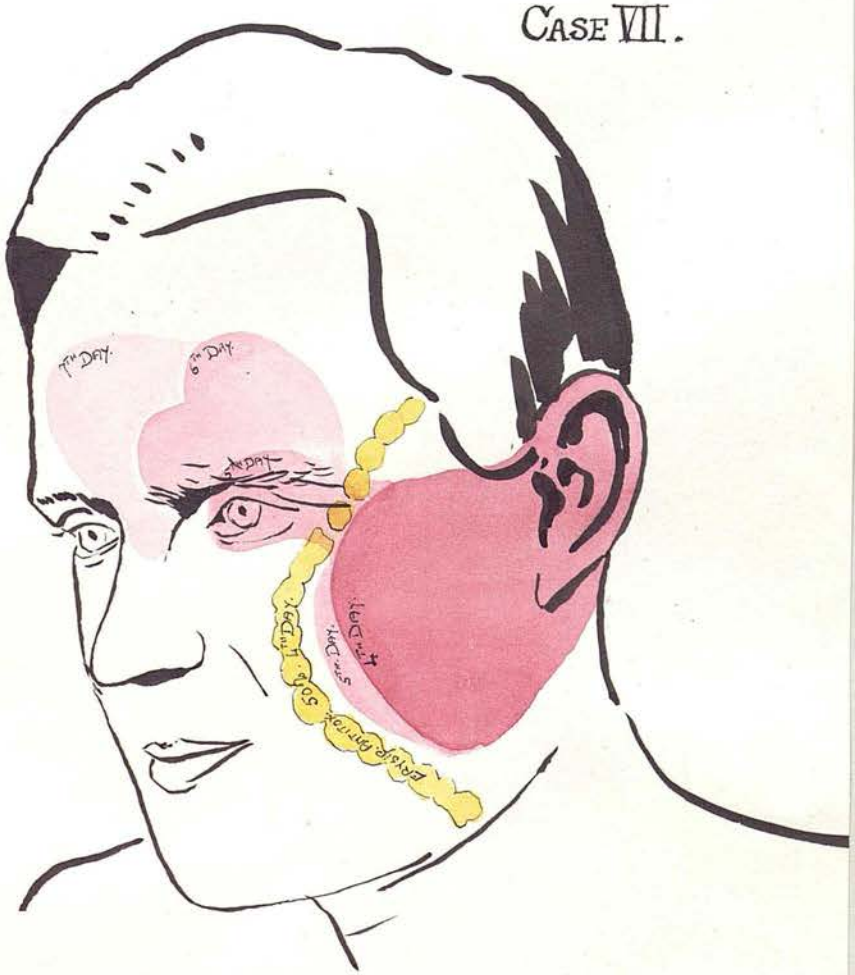
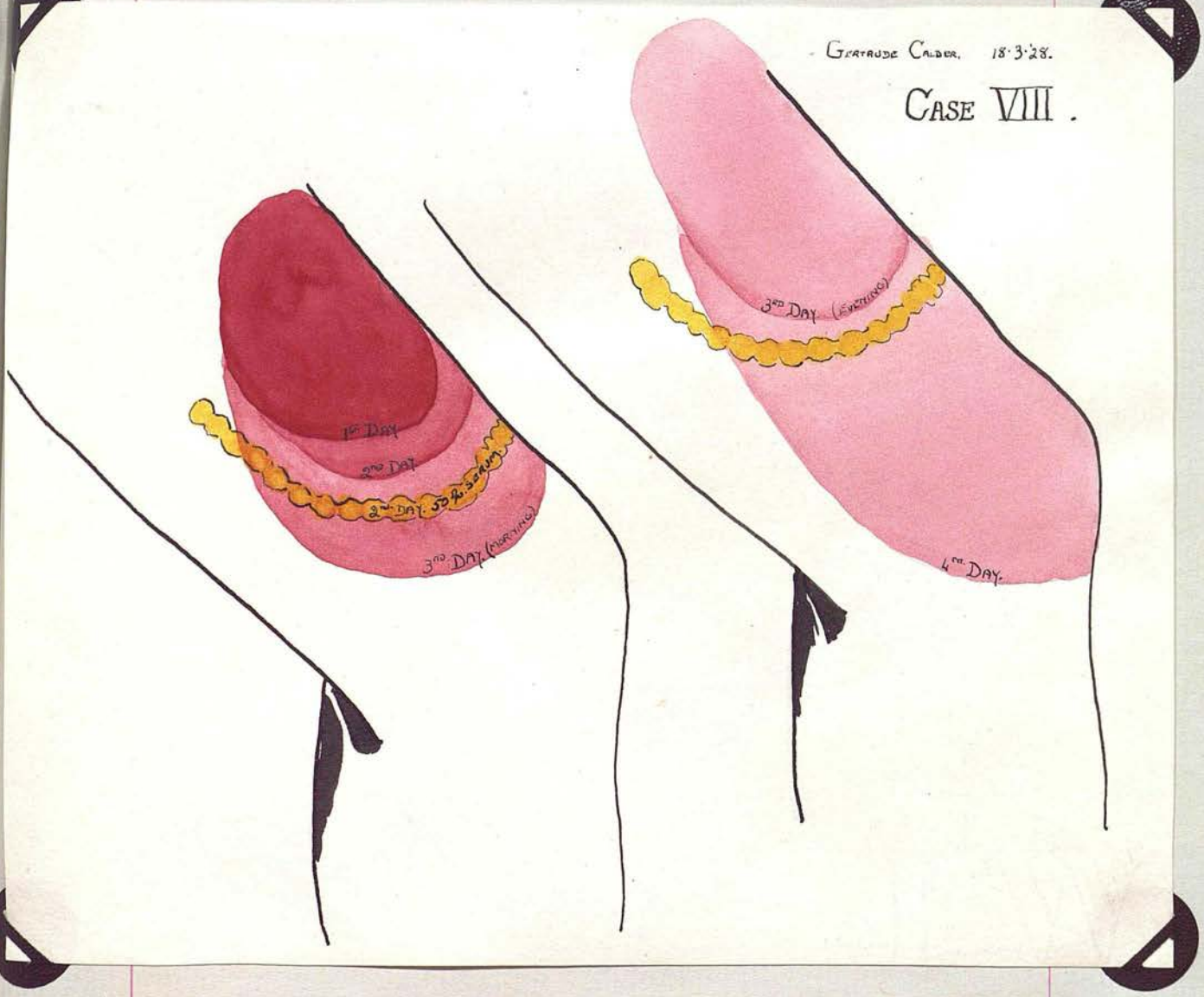
CASE VII.



Case 8 : Girl aged twelve years admitted with a sharp attack of scarlet fever and treated with

scarlet fever antitoxin on the second day of the disease. This was followed by a very well marked serum reaction six days later with fever and an urticarial rash.

Convalescence was slow and two months after admission she developed a patch of erysipelas on the inner aspect of the left thigh which spread slightly down the leg in the course of the first forty eight hours.



Serum and normal saline, one to one, were injected as shown and twelve hours later, the third day of the disease, redness and slight swelling were

found to have extended about one inch beyond the infiltrated area. That same evening it was discovered that the redness and swelling had receded to a line just proximal to the infiltrated area and there was an extremely well marked local urticarial rash. The question was then raised as to whether the apparent spread had not been a serum phenomenon with the erysipelas remaining quiescent in its previous site. In another twenty four hours, however, there was no doubt that the erysipelas had spread right down over the intradermal line and was involving the skin of the knee cap. From that date it subsided rapidly.

COMMENT.

From such a limited number of cases it is not possible to come to any definite decision as to the value of this form of treatment. Nevertheless it would appear to be worthy of further investigation.

The method is of interest when contrasted with a somewhat similar use of scarlet fever antitoxin, a serum of proved clinical value and considerable specificity. Scarlet fever antitoxin diluted so far as one to ten with normal saline will still cause a very define blanching of the already formed rash of scarlet fever, while this serum diluted with only one volume of saline is not too efficacious in preventing the spread of the erysipelatous lesion into skin protected some hours before. This comparison must not be carried too far, as, of course, the two rashes are hardly analogous. The scarlet fever rash being a toxic phenomenon whereas that of erysipelas is a local inflammatory reaction.

Our one experiment with diphtheria antitoxin is of interest in that it suggests that possibly this too, was effective in delaying the local spread. If this was the case, search for the explanation of the local action of the serum would of necessity be turned from the specific to the non specific element in the serum.

Further experiments to try to stop the spread by

means of normal horse serum are being carried out in the hospital at the present moment.

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SUMMARY AND CONCLUSIONS.

The (corrected) results of the treatment of 68 cases of erysipelas by erysipelas streptococcus antitoxin are detailed.

In this limited series of cases it would appear that the serum in no way reduced the fatality of the disease, shortened the period of fever, ameliorated the toxic depression, or stopped the local spread.

A procedure used to limit the local spread of the lesion is described and it is suggested that in suitable cases this is worthy of trial.

I have to thank Dr Benson, Superintendent of the City Hospital, Edinburgh, for permission to quote these cases and for much valuable help in the course of the investigation.

I am likewise indebted to Messrs. Parke Davis and Company for supplies of the serum when still in its experimental stage.

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